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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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STITES & HARBISON PLLC 1199 NORTH FAIRFAX STREET SUITE 900 ALEXANDRIA, VA 22314				PALENIK, JEFFREY T
ART UNIT		PAPER NUMBER		
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/520,657	GREF ET AL.	
	Examiner	Art Unit	
	Jeffrey T. Palenik	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 29 January 2008.
 2a) This action is **FINAL**. 2b) This action is non-final.
 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1-15 and 24 is/are pending in the application.
 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
 5) Claim(s) _____ is/are allowed.
 6) Claim(s) 1-15 and 24 is/are rejected.
 7) Claim(s) 11 is/are objected to.
 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
 10) The drawing(s) filed on 10 January 2005 is/are: a) accepted or b) objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ . |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>30 June 2005</u> . | 6) <input type="checkbox"/> Other: _____ . |

DETAILED ACTION

Response to Arguments

The Examiner thanks the Applicants for their timely reply filed on 29 January 2008, in the matter of 10/520,657.

Applicants' election **with traverse** of Group I, claims 1-15 and 24 is acknowledged. Applicants' election **with traverse** of C12 aliphatic groups (claim 7) and the first polymer association recitation of claim 9 are also acknowledged. Applicants traverse the election requirements on the grounds that the subject matter claimed, in view of that which is taught by Kosak et al. (USPN 6,048,736) is both novel and non-obvious. Applicants' further traverse on the grounds that “[c]laim 1 is a linking claim which unifies all of the claims in the present application to a single general inventive concept, namely an aqueous composition of a polymer/polysaccharide dispersion of particles”.

Applicants' remarks have been fully considered and are found to be persuasive. However, after further consideration of the prior art, a new lack of unity follows wherein the inventions listed in Groups I-III still do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding technical feature(s) because Amiel et al. (*Stimuli-Responsive Water Soluble and Amphiphilic Polymers -- ACS Symposium Series; Chapter 4*) expressly teach the composition and properties thereto of the claimed invention of Group I.

Applicants' elections of Group I and the respective species, as discussed above, stand. Furthermore, claims 16-2 (Group II) and 21-23 (Group III) remain withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a non-elected invention and

species, **there being no allowable generic or linking claim** (emphasis added). Applicants timely traversed the restriction (lack of unity) requirement between the particle composition and the distinct compositions comprising said particle composition.

The remaining claims 1-15 and 24 are presented and represent all claims under consideration.

Information Disclosure Statement

An Information Disclosure Statement (IDS) filed 30 June 2005 is acknowledged and has been reviewed.

Drawings

The drawings are objected to under 37 CFR 1.83(a) because they do not clearly/fail to show the details of the instantly claimed invention as described in the specification. Any structural detail that is essential for a proper understanding of the disclosed invention should be shown in the drawing. MPEP § 608.02(d). Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as “amended.” If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for

consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either “Replacement Sheet” or “New Sheet” pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

In addition to Replacement Sheets containing the corrected drawing figure(s), applicant is required to submit a marked-up copy of each Replacement Sheet including annotations indicating the changes made to the previous version. The marked-up copy must be clearly labeled as “Annotated Sheets” and must be presented in the amendment or remarks section that explains the change(s) to the drawings. See 37 CFR 1.121(d)(1). Failure to timely submit the proposed drawing and marked-up copy will result in the abandonment of the application.

Specification

Applicant is reminded of the proper content of an abstract of the disclosure.

A patent abstract is a concise statement of the technical disclosure of the patent and should include that which is new in the art to which the invention pertains. If the patent is of a basic nature, the entire technical disclosure may be new in the art, and the abstract should be directed to the entire disclosure. If the patent is in the nature of an improvement in an old apparatus, process, product, or composition, the abstract should include the technical disclosure of the improvement. In certain patents, particularly those for compounds and compositions, wherein the process for making and/or the use thereof are not obvious, the abstract should set forth a process for making and/or use thereof. If the new technical disclosure involves modifications or alternatives, the abstract should mention by way of example the preferred modification or alternative.

The abstract should not refer to purported merits or speculative applications of the invention and should not compare the invention with the prior art.

Where applicable, the abstract should include the following:

- (1) if a machine or apparatus, its organization and operation;
- (2) if an article, its method of making;
- (3) if a chemical compound, its identity and use;
- (4) if a mixture, its ingredients;
- (5) if a process, the steps.

Extensive mechanical and design details of apparatus should not be given.

Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

The abstract of the disclosure is objected to because of the reference to the lack of any figures. The recited phrase "Figure: none" should be removed.

Correction is required. See MPEP § 608.01(b).

Claim Objections

Claim 11 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The claim recites that at least 80% by mass of the

compounds (A) and (B) are present in the particles of the composition. This fails to further limit the composition of claim 1, which already recites that the particles contain compounds (A) and (B). For the purposes of examination on the record, the Examiner broadly and reasonably interprets claim 11 and reciting the same subject matter as claim 1.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Independent Claim 1 and dependent claims 2-15 and 24 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter that is not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Claim 1 is drawn to a composition comprising a dispersion of particles which contain, in association, polycyclodextrin molecules and macromolecules of polysaccharides which comprise “groups (G)” wherein said groups are capable of forming inclusion complexes with the cyclodextrins. Claim 7 further defines said “groups” as being aliphatic groups, linear or branched, having 8-18 carbon atoms. As discussed above, the Examiner acknowledges Applicants’ election of C₁₂ aliphatic groups. However, the Examiner further acknowledges that neither the term “groups” nor “C₁₂ aliphatic groups” is mentioned in the instant specification, the term is not defined by the instant specification in a clear and concise manner. As such, the disclosure of

the instant specification is not sufficient to support either of the generic concepts of “groups” or “C₁₂ aliphatic groups” and requires further clarification. As construed in the prior art, the Examiner is interpreting the term “group” to mean any chemical formulation found to associate with polysaccharides or polysaccharide macromolecules (See US Patent 6,048,736; column 12, lines 6-20).

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-15 and 24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The phrase “contain, in association” as recited in claim 1, renders the claims indefinite since it is unclear exactly how the polycyclodextrin molecules and polysaccharide molecules are structurally related. Given its broadest reasonable interpretation for the purposes of examination on the merits, the Examiner interprets the above phrase as “comprising”.

The phrase “at least” as recited in claims 1, 3, 11, 12 and 14, renders each of the claims indefinite because, in each instance, the phrase precedes a single numerical value (e.g. a percent, a number of cyclodextrin units, etc.), thereby reciting an ambiguous and open-ended range limitation (see MPEP §§2163.05(III) and 2173.05(II)). Read broadly, the claims where the numerical values represent percentages, the claims can be reasonably argued as reciting a composition comprising 100% by weight of the respective component.

Regarding claim 1, the phrase "capable" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d). Herein, and for the purposes of examination on the merits, the Examiner broadly and reasonably interprets part (B) of the composition as reciting macromolecules of polysaccharides.

Claim 8 recites the limitation "the rate of grafting" in line 2 of the claim. There is insufficient antecedent basis for this limitation in the claim.

The elected limitation of claim 9 makes the following recitation: "...polymers (A) having from 18 to 1000 β -cyclodextrin units / polysaccharides (B) of molecular mass between..." Said limitation renders the claim indefinite. It is unclear what ratio Applicant is claiming since the number of β -CD units per polysaccharide units is not clearly set forth. Herein, and for the purposes of examination on the merits, the Examiner broadly and reasonably interprets the elected limitation of claim 9 as reciting "from 18 to 1000 β -cyclodextrin units per at least one polysaccharide unit".

Regarding claim 13, the phrase "capable" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d). Herein, and for the purposes of examination on the merits, the Examiner broadly and reasonably interprets the particles as further comprising at least one additional chemical compound (C) as recited in the preceding instant claim 12.

Regarding claim 14, it is unclear as to how much of the composition is actually attributed to the compound (C). In addition to the aforementioned regarding the phrase "at least", the claim is further rendered indefinite since the quantity of compound (C) is "at least

0.5%” by mass relative to an indefinite total mass of particles. Herein, and for the purposes of examination on the merits, the Examiner broadly and reasonably interprets the limitation of claim 14 in the same scope of claim 12. The recitation is further read broadly on the grounds that Applicants indefinitely claim the number of additional chemical compounds comprising compound (C) (i.e. an open-ended range limitation, as discussed above).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-15 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Amiel et al. (*Stimuli-Responsive Water Soluble and Amphiphilic Polymers -- ACS Symposium Series; Chapter 4: “Macromolecular Assemblies Generated by Inclusion Complexes between Amphiphilic Polymers and β-Cyclodextrin Polymers in Aqueous Media”*).

The instant claims are directed to a composition comprising an aqueous dispersion of 50-5,000 nm diameter particles comprising (A) polycyclodextrin molecules of 4 or more units and (B) macromolecules of polysaccharides (claims 1, 5, 8, 11 and 24). Claims 5 and 24 both recite limitations which are deemed product-by-process limitations, which per MPEP §2113, hold no patentable weight towards the composition itself. Claim 1 recites an additional limitation wherein the compounds (A) and (B) are independently water-soluble. These solubility limitations are chemical properties which are examined as being inseparable from their respective chemical components (see MPEP §2112.01(II)). Similarly, limitation to the rate of grafting as recited in claim 8 is also interpreted by the Examiner as an inseparable property of the polysaccharide(s) of claim 1. Claim 2 further limits the diameter of the particles. Additional limitations to polymer (A) are recited such as the number of cyclodextrin units, the type of cyclodextrin, and the molar mass of the polymer (claims 4-6). The limitation of claim 7, recites that the groups (G) are linear or branched aliphatic groups having 8-18 carbon atoms. The limitation of claim 9 recites a concentration range of 18-1000 β -CD units per polysaccharides (B), wherein the polysaccharides range from 3-5% in their hydrophobic substitution and 6,000-70,000 in their molecular mass. Claim 10 recites a ratio limitation for cyclodextrin to aliphatic chains of the polysaccharides. The particles are recited as having at least one additional compound (claims 12-14), wherein the compound has a cosmetic or therapeutic effect (claim 15).

Amiel et al. teach that compositions comprising a variety of structures of host-guest polymers (e.g. inclusion complexes) wherein the host comprises β -cyclodextrin polymers (e.g. supramolecular β -CD) complexed with amphiphilic guest polymers which themselves

comprise hydrophobically modified dextran molecules (Title and Abstract, pp. 58-59 and ¶1 of pg. 59). Said hydrophobic modifications are taught as comprising rigid (e.g. adamantyl groups) or flexible structures (e.g. alkyl chains with more than 12 carbon atoms) (Abstract, pg. 58). Figure 3 on page 62, teaches the structure of some of the hydrophobic groups which may be used, the last of which is a linear, aliphatic 12-carbon carboxylate group. Both components are taught as being individually water soluble (see Abstract, pg. 58 and ¶1, pg. 64). Polymers of β -CD are taught wherein oligomeric β -CD contains an average of 3-4 units, low molecular weight polymers contain an average of 15 units, and high molecular weight chains contain more than 1000 units (pg. 65, *β -Cyclodextrin Polymers*). Table III teaches that the high molecular weight β -CD polymers will range in weight from 210,000 to 1,100,000 and comprise 87% w/w of the molecule. Since the Table does not say anything as to whether the β -CD molecules contain any molecules of hydrophobically modified dextran, it is interpreted that the 87% w/w value is β -CD alone. Table II (pg. 64) teaches various embodiments of Dextran-adamantane (Dext-Ad) and Dextran-alkane (Dext-Alk) and their properties. For instance, alkane-modified dextran polymers are taught as having a molecular weight of 40,000 and hydrophobic molar ration (e.g. hydrophobic substitution rate) ranging from 2.8-5.1%. Inclusion complex interactions are further taught such that the interaction strength of the overall chain is able to be tailored based on the number of β -CD cavities (e.g. empty units) available in the chain, the number of which ranges from 3-1000 in the chain (pp.70-71, *Aggregation in Solution*). Figure 2 depicts a polymer chain comprising β -CD polymers both hydrophobically modified and vacant at the instantly claimed ratio. Figure 9 (pg. 71) teaches a 1:1 ratio of total β -CD units to aliphatic chains present by way of

substituents on the polysaccharide macromolecules. More specifically taught is a 50/50 mixture comprising branched-aliphatic, hydrophobically-substituted Dext-Ad ($M_w = 500,000$; 2.4%Ad) and β -CD/EP. Amiel et al. also teach that the polymer of inclusion complexes may comprise at least one additional chemical compound such as polyethylene oxide (PEO), which may alternatively be complexed with the hydrophobic alkyl group and further complexed with β -CD molecules (Tables II-IV). Furthermore, the last paragraph of the Conclusion teaches that the guest molecule may also be a drug (pg. 80).

Amiel et al. do not expressly teach the instantly claimed particle ranges.

In view of the teachings of the prior art, one of ordinary skill in the pharmaceutical or biomedical art, at the time of the invention, would have been motivated to create a complex comprising supramolecular, β -cyclodextrin chain polymers, dextran molecules hydrophobically modified with 12-carbon aliphatic groups, and a therapeutic or cosmetic agent to achieve the claimed aqueous dispersion of particles. Such would have been obvious in the absence of evidence to the contrary since the Chapter 4 article of the *ACS Symposium* expressly teaches hydrophobically modified water soluble polymers and their association as “guest” polymers with their “host” β -CD polymers, polymer structures and sizes, as well as favorable inclusion of hydrophobic drugs as guest molecules.

A person of ordinary skill in the art would have a reasonable expectation of success in modifying the teachings presented by Amiel et al. to prepare the instantly claimed aqueous dispersion of polymer/polysaccharide particles since the Symposium article discloses the instantly claimed composite preparation method. Therefore, the invention as a whole would

have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention.

The reference does not expressly teach the hydrodynamic diameter of the dispersed particles, as claimed by Applicants. Since the values and formats of each parameter with respect to the claimed composition are adjustable, it follows that each is a result-effective parameter that a person having ordinary skill in the art would routinely optimize.

Optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art to employ. Amiel et al. do teach a relationship of adamantane concentration to hydrodynamic radius whereby β-CD/EP polymer coils which are complexed with polyethylene oxide-adamantane molecules (PEO-Ad) demonstrate radii values of 25-30 nm (e.g. diameters of 50-60 nm). Additional properties such as dimensions of the individual β-CD units (Figure 1) as well as generic schematic representations of β-CD polymerized as inclusion complexes with hydrophobically modified polymers (Figure 2) are taught. Thus, it would have been customary for an artisan of ordinary skill, to be able to adjust the hydrodynamic diameter of the particles as a result of adjusting the arrangement and quantity of β-CD as well as the concentration of the modified polysaccharide with which it is complexed. Thus, absent some demonstration of unexpected results from the claimed parameters, optimization of any of these parameters would have been obvious at the time of Applicants' invention.

All claims have been rejected; no claims are allowed.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey T. Palenik whose telephone number is (571) 270-1966. The examiner can normally be reached on 7:30 am - 5:00 pm; M-F (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jeffrey T. Palenik/
Examiner, Art Unit 1615

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